REMARKS

The amendments to the claims find support in the application as originally filed. The amendments to claims 1, 3, 5, 11, 14, 16, and 19-21 find support in the application as originally filed, for example, at page 23, lines 28-40 to page 24, lines 1-8 (paragraphs 120-121 on page 13 as published in U. S Patent Publication 20020081299); page 26, line 36 to page 25, line 29, and page 28, lines 2-33 (paragraphs 138-151 and 153-159 on page 15 as published in U. S. Patent Publication 20020081299), including particularly page 28, line 31 (paragraph 159, lines 9-10 of the paragraph, as published in U. S. Patent Publication 20020081299); and elsewhere in the specification and claims as originally filed.

Claims 2, 3, 5, 9, 13, 15, 17, and 18 stand canceled without acquiescence to any rejection of record and without prejudice to the prosecution of the subject matter in related continuation and divisional application

No new matter is added by way of the amendments to the specification or to the claims.

Claims 1-12, 14-17 and 19-21 are pending in the application, and stand rejected. Claims 1-12, 14-17, and 19-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. Claim 9 separately stands rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. Claims 1-12, 14-17, and 19-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement.

Claims 2, 15, and 17 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite.

Claims 1-5, 7, 8, 10-12, 14-17, and 19-21 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. 6,017,886 to Carnahan (hereafter "Carnahan") in view of U.S. Patent 5,367,060 to Vandlen *et al.* ("Vandlen"). Claims 1, 2, 10, 12, 14-17,

and 19-22 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Carnahan in view of U.S. Patent 5,587,458 to King (hereafter "King").

Applicants respectfully traverse the claim rejections.

The Rejections of Claims 1-12, 14-17, and 19-24 under 35 U.S.C. §112, first paragraph

Claims 1-12, 14-17, and 19-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement.

Applicants note that the USPTO states that the specification is "enabling for methods comprising contacting an inner-ear-supporting cell with heregulin molecules and fragments that comprise a growth factor domain, or certain specifically defined variants thereof" (page 6, paragraph "8.", lines 9-11 of the instant Office Action). Applicants note that the claims, as amended, are directed to methods comprising contacting an inner-ear-supporting cell with heregulin molecules that comprise a growth factor domain (comprising amino acid residues 175-230) or certain specifically defined variants thereof (at least 95% sequence identity; N-terminal and C-terminal cleavage points adjacent to an arginine, lysine, valine, or methionine residue; insertions, deletions or substitutions at residues specifically recited in the claims as disclosed in the specification). Applicants note that such fragments and variants are taught in the application (see, e.g., page 23, line 28 to page 24, line 8; page 26, line 36 to page 25, line 29, and page 28, lines 2-33). Applicants note further that the heregulin fragments and variants of the claims are required by the claims to be "effective to activate HER2 and/or HER 3 receptors."

Thus, the pending claims are seen to meet the criteria acknowledged by the USPTO as being enabled by the specification. Accordingly, Applicants submit that the claims are enabled by the specification as required by 35 U.S.C. §112, first paragraph, and that the rejections to claims 1-12, 14-17, and 19-24 as allegedly failing to comply with the enablement requirement under 35 U.S.C. §112, first paragraph are overcome.

The Rejection of Claim 9 under 35 U.S.C. §112, first paragraph

Claim 9 separately stands rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. However, claim 9 standing canceled without prejudice in the present amendment, Applicants believe the rejection of claim 9 under 35 U.S.C. §112, first paragraph to be moot.

The Rejections of Claims 1-12, 14-17, and 19-24 under 35 U.S.C. §112, first paragraph

Claims 1-12, 14-17, and 19-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement.

Applicants note that the claims, based on explicit recitations in the application as originally filed, describe the heregulin molecules required for the claimed methods. These heregulin molecules comprise a growth factor domain (comprising amino acid residues 175-230); variants satisfying the claim requirements are specifically (at least 95% sequence identity; N-terminal and C-terminal cleavage points adjacent to an arginine, lysine, valine, or methionine residue; insertions, deletions or substitutions at residues specifically recited in the claims as disclosed in the specification). Such fragments and variants are taught in the application (see, e.g., page 23, line 28 to page 24, line 8; page 26, line 36 to page 25, line 29, and page 28, lines 2-33). Applicants note further that these heregulin fragments and variants, which comprise specifically recited amino acid sequences and residues allowing of variation, are further required by the claims to be "effective to activate HER2 and/or HER 3 receptors."

Thus, the heregulin molecues that satisfy the requirements of the claimed invention are disclosed and described with precision in the application. Applicants respectfully submit that the rejections to claims 1-12, 14-17, and 19-24 as allegedly failing to comply with the written description requirement under 35 U.S.C. §112, first paragraph are overcome.

The Rejections of Claims 1-5, 7-12, 14-17, and 19-21 under 35 U.S.C. §112, second paragraph

Claims 2, 15, and 17 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. However, claims 2, 15, and 17 standing canceled without prejudice in the present amendment, Applicants believe these rejections to be moot.

Thus, the Applicant respectfully submits that the rejections to claims 2, 15, and 17 as allegedly indefinite under 35 U.S.C. §112, second paragraph are overcome.

The Rejections of Claims 1-8, 10-12, 14-17, and 19-24 under 35 U.S.C. §103(a)

Claims 1-8, 10-12, 14-17, and 19-24 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent 6,017,886 to Carnahan ("Carnahan") in view of U.S. Patent 5,367,060 (hereafter "'060"). The USPTO suggests that "it would be obvious ... that any heregulin peptide that retains a significant portion of the EGF-like domain can stimulate utricular sensory epithelial cells" (page 11 of the instant Office Action).

In order to establish a prima facie case of obviousness, there must be 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants note that the present invention, claims 22-24 in particular, are not limited to *utricular* cells, so that the applicability of the present rejection is unclear. However, Applicants note that the present claims do not recite, and do not encompass, "any heregulin peptide" but instead are directed to methods utilizing heregulin

fragments and variants thereof that meet explicit and restrictive criteria recited in the claims. Moreover, no combination of references suggests that fragments of a single heregulin molecule, or variants thereof, could be effective in the present methods.

In particular, the cited references, even if combined, lack disclosure or suggestion of the heregulin fragments and variants of the claimed invention, and so fail to provide all the elements of the claimed invention. Lacking these elements, and lacking any suggestion or motivation to provide these elements, there is no motivation to combine these references in an attempt to provide the claimed invention. Even if the cited references were to be combined in the absence of any teaching or motivation to do so, they would fail to provide the present invention with all the limitations of the pending claims. Thus, the combined references fail to provide any reasonable expectation of success for the combination. Carnahan, which requires a fusion protein including sequences from two different heregulins, teaches away from the present invention, which requires heregulin fragments from a single heregulin molecule instead of a combination from two different heregulins. Neither reference suggests the N-terminal or C-terminal sites of the present invention, nor does either reference suggest the sites named as suitable for substitution, deletion, or insertion.

Accordingly, Carnahan, discussing the use of hybrid fusion proteins of fragments from different heregulins to stimulate utricular sensory epithelial cells, and the '060 patent each fail to provide the isolated ligands used in the methods of the present invention, and the combination of these references fails to provide the isolated ligands used in the methods of the present invention.

Accordingly, the cited references lacking any motivation or suggestion to be combined to provide the claimed invention, and lacking any reasonable expectation of success for such a combination, Applicants respectfully submit that the rejections of claims 1-8, 10-12, 14-17, and 19-24 under 35 U.S.C. §103(a) is overcome.

The Rejections of Claims 1, 2, 10, 12, 14-17, and 19-22 under 35 U.S.C. §103(a)

Claims 1, 2, 10, 12, 14-17, and 19-22 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Carnahan in view of U.S. Patent 5,587,458 to King (hereafter, "King").

Carnahan is presented as discussing "all the target cell and intended use limitations" and King is presented as teaching the construction and use of antibodies that bind and activate erbB2 (HER2), referring to the Abstract of the King reference.

However, as discussed above, Carnahan lacks disclosure or suggestion of the heregulin fragments and variants of the claimed invention, and so, even in combination with King, fails to provide the present invention with all the limitations of the pending claims. Thus, Carnahan does not discuss "all the target cell and intended use limitations" of the present invention. Applicants note that the pending claims do not recite antibodies, the amendments to the claims being made without acquiescence to any rejections and without prejudice to prosecution of omitted subject matter in related continuation, continuation-in-part, and divisional applications. Thus, even though King is presented as teaching the construction and use of antibodies that bind and activate erbB2 (HER2), such a teaching, even if present, and even in view of Carnahan, fails to make the present claims obvious, as the present claims are not directed to such subject matter.

Moreover, King and Carnahan being directed to different arts, different cell types, and diametrically opposed goals, there is no suggestion or motivation in King to be combined with Carnahan. Thus, there is no suggestion or motivation in Carnahan, King, or in the art, to combine these references in order to provide the claimed methods.

Being so opposed, and being directed to different ends, there is no reasonable expectation of success for such a combination, were it to be made. The combination of Carnahan with King fails to discuss or suggest heregulin fragments and variants thereof as required by the claimed invention. Thus, even were these references to be

combined, the combination would not provide any reasonable expectation of success at providing the claimed methods.

Since the combination of the cited references fails to provide all the elements of the subject claim, and since the cited references provide no motivation to combine the cited references to provide the claimed invention, nor any reasonable expectation of success were the references to be so combined, applicants respectfully submit that claims 1, 2, 10, 12, 14-17, and 19-22 are not made obvious by the Carnahan in view of King, and that the rejections of Claims 1, 2, 10, 12, 14-17, and 19-22 under 35 U.S.C. §103(a) are overcome.

CONCLUSION

In view of the foregoing, it is respectfully submitted that all claims in the present application stand in condition for allowance. Applicant respectfully requests reconsideration and allowance of all claims. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **39766-0035 C1**.

Respectfully submitted,

Date: July 2, 2007

By: _____
James A. Fox (Reg. No. 38,455)

Heller Ehrman LLP
275 Middlefield Road
Menlo Park, California 94025-3506
Direct Dial: (650) 324-6951
Facsimile: (650) 324-6654